(11) 449029

PATENT SPECIFICATION (21) 19250/70

Class (52) 37.2; 57.2; 87.18; 87.16; 57.41.

Int. Cl. (51) A61d; A61k; A61j; B65d.

Application Number (21) 19250/70.
Lodged (22) 28th August, 1969.
(Accompanied by a Provisional Specification).

Complete Specification entitled (54) DEVICE FOR ADMINISTRATION TO RUMINANTS.

Lodged (23) 26th August, 1970.
Accepted (44) 17th May, 1974.
Published (41) 2nd March, 1972.

Convention Priority (30)

Applicant (71) COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION.

Actual Inventor (72) RALPH HENRY LABY.

Related Art (56)

248877(56171/60)	87.1.
410174(1457/66)	87.1.

The following statement is a full description of this invention, including the best method of performing it known to us :

X606-118-3D-41P.C.

F. D. Atkinson, Government Printer, Canberra

19250/70

This invention relates to devices suitable for administering to ruminants. More particularly, it relates to devices useful for preventing bloat in bovines, and for preventing other disorder of ruminants for which reticulorumen (hereinafter abbreviated to rumen) infusion of an effective curative or control agent over an extended period of time would be an advantage. Whilst particular reference is made hereinafter to devices for the prevention of bloat, it will be understood that these devices are equally applicable to the prevention of these other disorders. Thus, for example, the devices described herein provide a means for the perfusion into the rumen of the therapeutic substances, metal salts for the correction of deficiency diseases, or nutrients or other agents which may be of advantage for healthy stock.

Bovine bloat is characterised by distension of the animal's rumen and results from the formation of a stable foam above the rumen liquor which prevents the escape of gases produced by the micro-organisms in the rumen. Cattle feeding on fresh clover are particularly prone to bloat as stable foams are rapidly produced from certain clover proteins.

At the present time bloat may be prevented by daily administration of a surfactant to the animal, for example, in the form of a drench.

That method of prevention, however, is only truly practicable with dairy cattle since the cattle are brought in daily for milking; even here there is considerable farmer resistance to drenching because of the additional handling of the animals.

In general, that method is not feasible for beef cattle and thus there is a need for a prophylactic which can be administered to beef cattle at the commencement of the bloat season in order to allow the cattle to take advantage of lush pastures.

It is known to employ a variety of heavy pellets for prophylaxis in ruminant animals, for example, for correcting cobalt deficiency. These pellets rely upon their size and density so that they will remain within the rumen and upon their chemical composition for gradual dissipation of the active agent. It is difficult to apply this principle to the prevention of bloat since surfactants have a relatively low density and must be incorporated as a minor constituent in a large pellet weighted by a suitable inert material. The result is that very large quantities (3kg) of such pellets must be employed in order to furnish bloat protection for about three months - the period of the normal bloat season. If the weighting material is not used so that a high concentration of agent can be employed, it is found that such pellets can be readily regurgitated.

According to this invention there is provided a device for insertion into the rumen of a ruminant through the oesophagus and adapted to be retained within the rumen for free movement therein while releasing a therapeutic or nutrient substance at a substantially uniform rate over an extended period of time, said device comprising a body containing an effective amount of the therapeutic or nutrient substance, said device having a first compressed or closed configuration and a second expanded or open configuration, the first configuration permitting the passage of the device

through the oesophagus into the rumen and the second configuration being one which will substantially hinder passage of the device through the oesophagus but will still permit substantially free movement of the device with the rumen, and means for resiliently urging said device from said first configuration to said second configuration, whereby said device in said first configuration may be administered per os so as to pass into the rumen and will assume said second configuration in the rumen so as to hinder regurgitation during the said period, and will remain intact in said second configuration for the said extended period of time.

In one aspect, the device, the body by virtue of its nature, construction or composition, is itself adapted to be arranged in said first configuration and, in the rumen environment, to assume said second configuration.

In this aspect of the device, the body portion may comprise for example a substantially insoluble, resilient matrix material which contains or comprises a material to be released in the rumen. Such a material may be retained in the matrix material in the form of a suspension, solid solution or the like. Alternatively it may be weakly chemically bonded to the matrix material.

In a particular example of this aspect of the device, the body portion may consist of a gel comprising a material to be released in the rumen.

Such a gel may be moulded or otherwise formed into a body portion of a suitable shape whereby it is adapted to be arranged in said first configuration and, in the rumen environment, to change into said second configuration

as above mentioned. The gel may contain gelling agents and other components required to obtain the desired mechanical properties.

Suitable shapes into which the body portion may be formed include, for example, shapes which may be termed "doughnut-shaped" (i.e. toroidal) and "boomerang-shaped" (i.e. angular) and other similar shapes. Preferably the device is "doughnut-shaped."

In this particular aspect, the material to be

released in the rumen may be one or more non-ionic surfactant compounds.

The preferred surfactants are block copolymers of polyoxypropylene and polyoxyethylene, such as those manufactured under the ~~trade name~~ Registered trade mark "Pluronic", especially types L62, L62 and L64 thereof. Other polyoxyalkylenes and copolymers thereof are also suitable, as are polyoxyethylene alcohols (sometimes called polyoxyethylene alkyl ethers), i.e. consisting of straight or branched long chain alcohols condensed with ethylene oxide with or without end groups formed by condensation with propylene oxide. The condensation products of dodecanol with 6, 8, 10 or 12 moles of ethylene oxide are preferred members of this class.

~~Another type of~~ Other surfactants which may be used ~~is~~ are the polyoxyethylene alkylphenyl ethers, for example the condensation products of nonyl- or octyl-phenol with 8 or 9 moles of ethylene oxide, or with 9 to 11 moles of ethylene oxide followed by 9 to 11 moles of propylene oxide.

The preparation and properties of the above-described substances are well known in the art and will not be described herein.

The gelling agent may be of any suitable known type; ethyl cellulose is one example but the art discloses many other suitable substances.

In order to obtain a matrix material having the desired properties, the gel suitably contains at least 3% by weight, and preferably 6 to 15% by weight, of the gelling agent.

In another aspect, the device comprises at least one container portion and at least one obstructing means associated therewith, said obstructing means being arranged in a first position relative to the container portion to allow the device to be administered to a ruminant per os so as to pass into the rumen but which, in the rumen environment, moves or is caused to move relative to the container portion to a second position thereby to change the device into a second configuration as mentioned above.

The obstructing means may comprise for example one or more protruding or protusible structures attached to or formed integrally with the container portion and arranged so that (a) it may be positioned adjacent to the container portion, preferably more or less in conformity with the shape of the container portion, for passage of the device into the rumen, and (b) once in the rumen it can be caused or allowedto extend or protrude from the container portion and thereby obstruct or at least hinder passage of the device out of the rumen.

Thus the obstructing means may comprise one or more flaps, tabs, flanges or like projections, or loops, bubbles, blisters or like protuberances.

In an extension of the latter aspect, the obstructing means may comprise one or more further container portions.

Thus in yet another aspect of the invention, the device comprises at least two inter-connected container portions which are arranged relative to one another in a first configuration to allow the device to be administered to a ruminant per os so as to pass into the rumen thereof, and which, in the rumen environment, may be caused or allowed to move relative to one another to change the device into a second configuration as above mentioned. In this form of the device the container portions generally will be connected together by some connecting means which may take the form either of a simple hinge or like member which permits the container portions to move relative to one another but to remain essentially adjacent or it might comprise a member such as a web, string or rod which permits the container portions to separate from one another whilst still remaining connected. In the latter case, it is preferred that the connecting member is at least semi-rigid and capable of holding the container portions in the separated configuration.

Means may also be provided to positively assist or bring about the change in configuration of the device within the rumen environment. Such means may comprise the obstructing means or connecting means broadly described above or may consist of additional biasing means. For example, the obstructing or connecting means may be made of a suitable resilient material and arranged so that normally the obstructing or connecting means is biased towards its extended or protuberant position by virtue of its resilience. Alternatively the same function may be achieved by attaching the obstructing or connecting means

to its respective container portion by a hinge of resilient material or by a passive hinge provided or associated with biasing means.

The biasing means may be any suitable elastic or resilient material such as natural or synthetic elastomers or resilient synthetic resins, for example, natural or synthetic rubber, semi synthetic plastic materials such as cellulose esters, synthetic plastic materials such as the polyamides including nylon, polyethylene terephthalate, polyethylene and other similarly resilient materials or an elasticized cloth.

The means provided to assist or bring about the change in configuration of the device in the rumen environment may also be a strip comprised of a length or hydrophilic material and a length of hydrophobic material bonded or otherwise connected together. In the presence of moisture, such strips will deform as a result of expansion or contraction of the hydrophilic material. Such strips will hereinafter be referred to as "hydrophilic/hydrophobic strips". Alternatively, the means may be a strip or piece of a material which shrinks in the rumen environment.

Hydrophilic materials suitable for use in the hydrophilic/hydrophobic strips described above include cross-linked polydextrans, gelatin treated with formalin and cross-linked polyvinylalcohols. Suitable hydrophobic materials include water-insoluble polymers such as P.V.C., polyethylene and nylon.

A suitable material which shrinks in the rumen environment is cross-linked polyvinyl alcohol. This

material, if stretched when fully swollen with water and allowed to dry in the stretched state, will shrink when placed in the rumen environment.

Generally on administration the device will be held in the first configuration, by the throat of the animal but, if desired, restraining means may be provided which, in the rumen environment, are released to allow the device to move or be caused to move into the second configuration which will prevent or at least hinder passage of the device out of the rumen.

The restraining means may be or comprise any material which is dissolved, destroyed, ruptured or broken in the rumen environment. Suitable materials from which the restraining means may be made include gelatin string, gelatin tape and water-soluble adhesives.

As it is sometimes desirable to provide for the regurgitation of the device (if indigestible) by the animal, it is also preferred that the connecting means or hinge of the previously described embodiments comprise at least one soluble, corrodible or frangible element, which, after the device has ended its functional life, will dissolve, disintegrate or fracture to allow the device to fragment into smaller sections which are more readily regurgitated by the animal. For example, the hinge may be provided with a soluble or corrodible pin or secured to the container portion by a clip, button, link or trigger made of a corrodible or slowly soluble material. Suitable materials for this purpose will be obvious but by way of example there may be mentioned poly(vinyl alcohol), proteinaceous materials, e.g. casein, magnesium and its alloys, iron, steel and other

corrodible metals.

In a further aspect of the device, the actual containers are replaced by solid or semi-solid blocks comprising or consisting of the active substance. Where the substance to be released in the rumen is contained in one or more container portions, the device is normally constructed so that the material contained therein is released over an extended period of time. This may be achieved in a number of ways. For example, this material may be enclosed in a number of capsules having differing solubility in rumen liquor. Tablets of the material may be coated with other materials having differing solubility in rumen liquor. The container portions of the device may be permeable in whole or in part to the material or to rumen liquor, the permeability and amount of permeable material being such that the material contained in the container portions will be released into the rumen at the desired rate. Sustained release of a solid material may be achieved by using the material in the form of a sparingly soluble solid, the rate of dissolution of which gives the required rate of release of the material. The solid may be contained in the device behind an insoluble gauze, for example, of nylon, or a perforated or slotted plate of the container materials. Where the material to be released is a corrodible solid (for example magnesium metal for the control of grass tenany, as described hereinafter), it is preferred that the material is in the form of a hollow half-cylinder. This has the advantage that reduction in the surface area by corrosion from the outside or inside cylindrical surfaces is kept to a minimum throughout the lifetime of the device.

When liquid surfactants are to be administered by use of a device according to the invention having one or more container portions, it is preferred that sustained release is obtained by using the surfactant in the form of a gel, as has already been described. Other methods include encasing the surfactant in a permeable, water-insoluble materials having capillaries or interconnecting pores extending through them and paper or cloth partially impregnated with water-insoluble polymers such as cellulose acetate or polystyrene to reduce the permeability. Such permeable materials may be protected by water-destructable coatings. Films comprising water-soluble and water insoluble materials in which the water-soluble material will dissolve away in the rumen environment to make the film permeable, may also be used. Examples of such films are films of ethyl and methyl cellulose, the latter being soluble, and films of cellulose esters such as the acetone and poly (dimethylamino-ethyl methacrylate) or poly (tertbutylaminoethyl methacrylate) the latter materials being soluble in acids.

Materials which may be administered by use of the device according to the invention include not only liquid surfactants as mentioned above, but also other medicaments, dietary suppliments or concentrated nutrients, or combinations of any two or more of these materials. Examples of medicaments which may be administered include antibiotics, sulpha drugs, sedatives, anthelmintics, antipyretics, hormones, hypoglycemic agents, antispasmodics and hematics. Furthermore, the device may be used to release "rumen-by-pass" materials. These materials comprise an active material which has a coating of, or is incorporated in a matrix of, a polymeric material

which is unaffected in the rumen environment, but which is attacked and dissolved as the materials pass further down the digestive tract of the ruminant.

Suitable polymeric materials include polymers of formaldehyde or its condensation products, with amines and/or amides, polymers and copolymers of certain of the N-alkyl amino alkyl-acrylates, -methacrylates, -acrylamides and -methacrylamides and cyclic imides of copolymers of maleic anhydride and styrene, which are insoluble in the rumen environment.

As indicated above, the device may be used to prevent disorders of ruminants other than bloat. Such disorders include hypomagnesemia (grass tetany), hypocalcaemia (milk fever) and acetonaemia (ketosis, grass fever).

Hypomagnesemia and grass tetany are both manifestations of magnesium deficiency. They can occur in cattle, particularly during the early stages of lactation, when the daily intake of magnesium with their diet is less than the demands imposed by milk production. Administration of sufficient magnesium to prevent hypomagnesemia (1 to 3 g/day) generally eliminates the more severe milk fever. Both disorders may be manifest over the whole of the lactation period, but treatment with a magnesium supplement during the first 8 to 12 weeks is generally considered to be adequate in most cases. The use of the devices herein described for supplying supplementary magnesium is not restricted by the requirement of a high density as are the known pellets for preventing these disorders. Consequently, a wider selection of

magnesium compounds as potential prophylactics may be made. For example, magnesium oxide (periclase), hydroxide (brucite) laurate, oxalate, and other compounds or mixtures of compounds may be used to provide the required daily supplement of magnesium.

It will be appreciated that while passage of the presently known pellets from the rumen further down the digestive tract does not appear to be likely, the configuration to which a device according to the invention is changed in the rumen environment will also prevent or hinder passage of this device further down the digestive tract.

The present invention also extends to methods of treating ruminants which comprise the steps of administering to the ruminant, per os, a device according to the invention or a plurality of such devices.

Several examples of devices in accordance with this invention will now be described with reference to the accompanying drawings in which:-

Figure 1 is an exploded perspective view of one half of a preferred form of the device;

Figure 2 is an end elevation and Figure 3 is a sectional view of the device of Figure 1, in the first and second configurations respectively;

Figures 4 and 5, 6 and 7, 8 and 9 are sectional views of other devices in the first and second configurations respectively;

Figures 10 and 11, 12 and 13 are plan and sectional views of another embodiment in the first and second configurations, respectively.

The "first configuration" of the devices refers to that configuration in which they are adapted to be passed via the oesophagus of a ruminant into the rumen, and the "second configuration" to that adopted once in the rumen.

The device shown in Figures 1 to 3 comprises two boat-like semi-cylinders 1 which are 6" to 7" long and have semi-hemispherical ends. When placed together they form a 1½" diameter cylinder with rounded ends, and having two filling spouts 2.

The semi-cylinders are made of an impermeable and water-insoluble polymer, such as cellulose acetate, polypropylene or polyethylene. They may, if desired, be reinforced with paper or other fibres, or cloth.

The flat face of each semi-cylinder 1, is comprised by a plate 3 having a half-inch slot 4 therein, provided with a curved inwardly directed lip 5.

The plate 3 also has a projecting tab 6 provided with a slot 7. A male hinge member 8 and a female hinge member 9 are attached to or moulded integrally with the edge of the plate 3 carrying the tab 6. The male hinge member 8 comprises an outwardly projecting spigot 8A carrying a short pin 8B. The female hinge member 9 comprises a spaced pair of spigots 9A having pin-receiving slots 9B in their outer ends.

As shown in Figure 3, the device is also provided with a trigger mechanism comprising corrodible metal washer 10 attached to the outside wall of each semi-cylinder 1 by an expanded spigot 11. A circumferential groove 12 runs from the spigot 11 around the semi-

cylindrical face of each semi-cylinder 1. A hinge link 13 (Figures 1 and 3) is provided to secure the two semi-cylinders 1 together. The link 13 consists of a strip of flexible plastics material having thickened end portions 13A with a hole 13B therein. If desired a narrow slit 13C may be provided between the hole 13B and an edge of the strip to facilitate assembly of the device as described hereinafter. In an alternative form of the link shown as 113 two holes 113B are provided, each with a slit 113C, communicating with edges of the strip. In use two semi-cylinders 1 are secured together as shown in Figure 3 by inserting the male hinge members 8 in the female hinge members 9. The link 13 is bent to a U-shape and one end portion is passed through the slot 7 in each semi-cylinder 1. One end of a band 14 of an elastic material, e.g. rubber, is looped around the spigot 11 and under the washer 10 on one of the semi-cylinders 1. The band 14 is passed along the groove 12 through the holes 13B in each end of the link 13 and then along the groove 12 of the other semi-cylinder and the other end of the band is looped around the spigot 11 of the other semi-cylinder.

Each of the semi-cylinders contains about 100 ml. of gelled "Pluronic" L62 (see Example 1). Other suitable antifoaming agents include polypropylene glycols, "Pluronic" L61 and L64, and products produced by condensing long chain alcohols with ethylene oxide, e.g. lauryl alcohol condensed with 6 to 12 moles of ethylene oxide.

As shown in Figure 2 the cylinders may be folded together to form an essentially cylindrical structure

against the tension of the band 14. The device may be retained in this configuration by means of a band of soluble material e.g. a gelatin tape, or alternatively the constriction of the oesophagus in the animal may be sufficient to provide the necessary restraint during administration. Once in the rumen the device opens to the configuration shown in Figure 3 thus allowing the contents of the rumen to contact the material contained in the semi-cylinders through the slot 4.

The washers 10 are made of magnesium or any similar corrodible metal and are proportioned so that at some time after the contents of the device have been released the pins will corrode to such an extent that they will release the ends of the band 14 from the spigots 11. The band 14 can then pull free of the link 13 which in turn can become detached from the slots 7 by the natural movement of the device within the rumen. The hinge members 8, 9 can then detach and the animal can regurgitate the individual semi-cylinders.

In an alternative arrangement the semi-cylinders 1 are filled with liquid "Pluronic" L62 or the like, and the flat faces are closed by a sheet of porous paper impregnated with cellulose acetate to reduce its permeability Other permeable materials or materials adapted to become permeable which could be used have previously been listed.

The device shown in Figures 4 and 5 is similar to the one shown in Figures 1 to 3, except that it has hemi-cylinders 21 which are closed on their straight sides and are made of permeable material or material adapted to become permeable. In lieu of hinges and

elastic bands, the hemi-cylinders 21 are connected to two hydrophilic/ hydrophobic strips 22 and as shown in Figure 4 are secured together by means of a gelatin tape 23. In the rumen, the gelatin tape 23 dissolves and the strips deform to the configuration shown in Figure 5, thereby to prevent or hinder regurgitation of the device.

A similar device can be constructed with three lobes which together make up a cylinder. In a further modification, elastic hinges, which have a rest position similar to that shown in Figure 5, and are deformed to a configuration similar to that shown in Figure 4 to allow the device to pass via the oesophagus into the rumen, may replace the hydrophilic/hydrophobic strips.

The device shown in Figures 6 and 7 is particularly

suitable for administering solid substances such as magnesium metal or gelled "Pluronic" surfactants. The two hemi-cylinders 31 are joined by an elastic hinge member 32 made out of nylon. The rest position of the hinge is as shown in Figure 7, but it is deformed into the configuration shown in Figure 6 to allow the device to pass via the oesophagus into the rumen. A gelatin tape 33 may be positioned as shown to secure the device in the configuration.

The devices shown in Figures 8 and 9 consist of a cylinder 41 having two substantially rigid, hemi-cylindrical "wings" 42, 43 respectively attached to the cylinder 41. Preferably, both the cylinder 41 and the wings 42, 43 have rounded ends. The cylinder 41 is made of permeable material or has slots to allow release of the active material. The wings 42, 43 are initially folded so as to fit closely around the cylinder 41, as shown in Figure 8, to allow the devices to pass via the oesophagus into the rumen. There, the gelatin tape 44 dissolves and the devices are changed to the configuration shown in Figure 9, thereby to prevent or hinder regurgitation.

The device shown in plan in Figures 10 and ~~13~~ 12 and in cross section in Figures 11 and 13, comprises a body portion 51 of a substantially insoluble resilient matrix material incorporating a material to be released in the rumen, moulded or otherwise formed into a "doughnut"-shape as shown in Figures 12 and 13. The body portion 51 may for example have an overall diameter of 4", the diameter of the inside cutaway portion being 2.8" and the maximum thickness 0.5". This device, before administration to the ruminant is deformed to the

configuration shown in Figures 10 and 11 and held in that configuration by gelatin tapes 52. When the device in this configuration is passed into the rumen, the rumen liquor causes the gelatin tape 52 to dissolve and the device, because of the resilience of the body portion, reverts to the configuration shown in Figures 12 and 13 thereby to prevent or hinder regurgitation of the device.

A suitable material from which the body portion 51 may be formed may be prepared by heating a liquid surfactant with 8% by weight of ethyl cellulose to a temperature of 160°C. to form a clear solution. This clear solution is poured into a suitable mould and cooled to form a rubber-like solid. A body portion formed in this way releases the surfactant slowly from the matrix material into the rumen environment. Liquid surfactants which may be incorporated into a matrix material in this way include the Pluronics L62 and L64 and the product formed by condensing 1 mol. of nonyl phenol with 11 mols.of ethylene oxide and further condensing the thus produced product with 11 mols. of propylene oxide.

The following examples show the use of some of the above described devices.

EXAMPLE 1

Plastic cylindrical capsules 150 mm long and 30 mm

diameter, made up of two half-cylinders hinged along one edge, were constructed. The hinges were of rubber and were biased so that two half-cylinders would spring apart in the rumen and thus expose flat surfaces of the half-cylinders through which the agent in the capsule could diffuse into the rumen. The hinges were constructed so that, under the rumen conditions, they would pull away from the half-cylinders after effective release of the agent, thereby facilitating regurgitation of the fragmented devices.

The capsules were filled with a gel of "Pluronic" L62 (90%) and ethyl cellulose (10%). Release of the surfactant from the gel was restricted by 9 x 130 mm slots in the flat face of the capsules.

A commercial herd of 46 milking cows, predominantly Jersey, were treated with two capsules each. Thirty further cows of the same herd were drenched at the evening milking with 7.5 ml of "Pluronic" L64. The cows grazed on irrigated pasture, predominantly white clover (Trifolium repens). Bloat was assessed visually, scores 1 to 3 being (1) left flank distended, (2) both flanks distended, and (3) in need of immediate treatment. The trial lasted for 28 days.

Preliminary experiments showed that half-cylinders and un-opened capsules of the quoted dimensions were regurgitated less than 48 hours after administration. The rate of release of surfactant from the capsules was approximately proportional to the amount remaining in the capsule, the half-life being 42 days. The mean release was 6g/cow/day.

No bloat was observed in the animals treated with the capsulesduring the first four days of the trial, while 5 cases of bloat were recorded for the drenched cows. Over the trial period 76% of the animals treated with the capsules and 47% of those drenched had bloated. Of the total number of bloated cases observed in the treated animals, 6% occurred during the first nine days, 24% during the next fifteen days and 70% during the final four days. The corresponding proportions in the drenched animals were 31%, 48% and 21%.

Regurgitated fragments of capsules were recovered in the fields from the first day after treatment; 34 half-cylinders and 9 smaller fragments were found. One intact capsule was found after the experiment concluded.

While these trials indicate some degree of success it was considered that the hinges of the capsules failed too quickly leading to premature regurgitation. However, it was clear that release of the surfactant from the retained capsules continued for about 25 days.

EXAMPLE 2

The experiment of Example 1 was repeated using capsules with strengthened hinges.

In this case 50 cows of the same herd as in Example 1 were treated with two of the devices and 16 further cows of the same herd were kept overnight in pastures sprayed with anti-bloat oil. The conditions of the experiment were similar to those of Example 1 and the trial last 36 days.

In the animals treated with the capsules, no bloat occurred during the first 11 days while 30 cases

were recorded for the animals on the sprayed pasture. Over the trial period 65% of the treated animals and 88% of those on spray pasture bloated.

The incidence of severe bloat (i.e. that requiring treatment of drenching with oil) per 1000 cow-days, in the animals treated with the capsules was reduced to 1% of that for the control animals over the first 32 days. The surfactant in the capsules was exhausted by the 36th day.

5 complete capsules and 3 fragments were recovered in the field over the trial period.

These results show that with a correctly constructed capsule substantial protection of cows against bloat can be achieved for extensive periods, and no treatment is required other than the initial administration of the capsules.

It is to be realised that modifications and adaptions may be made to the constructions specifically described above. For instance, use may be made of semi-permeable materials to cause configuration changes by osmotic swelling. ~~Accordingly, all such modifications and adaptions are to be considered as falling within the spirit and scope of this invention which includes every novel feature and combination of features disclosed herein.~~

The Claims defining the invention are as follows:-

1. A device for insertion into the rumen of a ruminant through the oesophagus and adapted to be retained within the rumen for free movement therein while releasing a therapeutic or nutrient substance at a substantially uniform rate over an extended period of time, said device comprising a body containing an effective amount of the therapeutic or nutrient substance, said device having a first compressed or closed configuration and a second expanded or open configuration, the first configuration permitting the passage of the device through the oesophagus into the rumen and the second configuration being one which will substantially hinder passage of the device through the oesophagus but will still permit substantially free movement of the device with the rumen, and means for resiliently urging said device from said first configuration to said second configuration, whereby said device in said first configuration may be administered per os so as to pass into the rumen and will assume said second configuration in the rumen so as to hinder regurgitation during the said period, and will remain intact in said second configuration for the said extended period of time.

2. A device as claimed in Claim 1, wherein the body by virtue of its nature, construction or composition, is itself adapted to be arranged in said first configuration and, in the rumen environment, to assume said second configuration.

3. A device as claimed in Claim 2, wherein the body portion is comprised of a substantially insoluble, resilient matrix material which contains or comprises a material to be released in the rumen and is of such shape that it may be arranged in said first configuration and, in the rumen environment, assume said second configuration.

4. A device as claimed in Claim 3, wherein the body portions is of essentially toroidal form.

5. A device as claimed in Claim 3 or Claim 4, wherein the body portion consists of or comprises a gel which contains the material to be released into the rumen.

6. A device as claimed in Claim 5, wherein the material is a bloat control agent.

7. A device as claimed in Claim 6, wherein the body portion comprises a polyoxyalkylene and ethyl cellulose as a gelling agent.

8. A device as claimed in Claim 7, wherein the gelling agent comprises at least 3% by weight of the gel.

9. A device as claimed in Claim 1, which comprises at least one container portion and at least one obstructing means associated therewith, said obstructing means being adapted to be arranged into a first position relative to the container portion to allow the device to be administered

to a ruminant per os so as to pass through the oesophagus and into the rumen and, in the rumen environment, to move relative to the container portion to a second position thereby to change the device into said second configuration.

10. A device as claimed in Claim 9, wherein the obstructing means comprises at least one protruding or protusible structure attached to or formed integrally with the container portion and arranged so that (a) it may be positioned adjacent to the container portion, for passage of the device through the oesophagus and into the rumen, and (b) once in the rumen, it can be caused or allowed to extend or protrude from the container portion and thereby to at least hinder passage of the device out of the rumen through the oesophagus.

11. A device as claimed in Claim 10, wherein the container portion is a cylinder and the said structure or structures conform substantially the shape of the cylinder for administration of the device and lie parallel to the longitudinal axis of the cylinder in the extended position.

12. A device as claimed in Claim 9 or Claim 10, wherein the obstructing means comprises at least one further container portion.

13. A device as claimed in Claim 12, comprising two part-cylindrical container portions which are connected by a web or webs, and which are arranged to form a cylinder

for administration and which in the extended position move apart but remain connected by the web and lie with their longitudinal axes essentially parallel.

14. A device as claimed in Claim 1, which comprises at least two inter-connected container portions which are arranged relative to one another in a first configuration to allow the device to be administered to a ruminant per os so as to pass through the oesophagus into the rumen thereof, and which, in the rumen environment, may be caused or allowed to move relative to one another to change the device into said second configuration.

15. A device as claimed in Claim 14, wherein the container portions are hemi-cylindrical and connected by a hinge along a common edge with their longitudinal axes parallel, and are arranged to form a cylinder for administration and to move apart about said common edge into the second configuration.

16. A device as claimed in any one of Claims 9 to 15, wherein the obstructing means is attached to the container portion by a soluble, corrodible or frangible element which is susceptible to destruction in the rumen environment, whereby after the device has ended its functional life the destruction of the element will allow fragmentation of the device.

17. A device as claimed in any one of Claims 9 to 16,

wherein the said substance is a bloat control agent.

18. A device as claimed in Claim 17, wherein the agent is a polyoxyalkylene.

19. A device as claimed in Claim 18, wherein the agent is selected from the class consisting of "Pluronic" L62, "Pluronic" L61, "Pluronic" L64 and the product of the condensation of lauryl alcohol condensed with 6 to 12 moles of ethylene oxide.

20. A device as claimed in any one of Claims 9 to 16, wherein the said substance is a source of magnesium.

21. Any one of the devices for administration to a ruminant substantially as hereinbefore described with reference to the accompanying drawings.

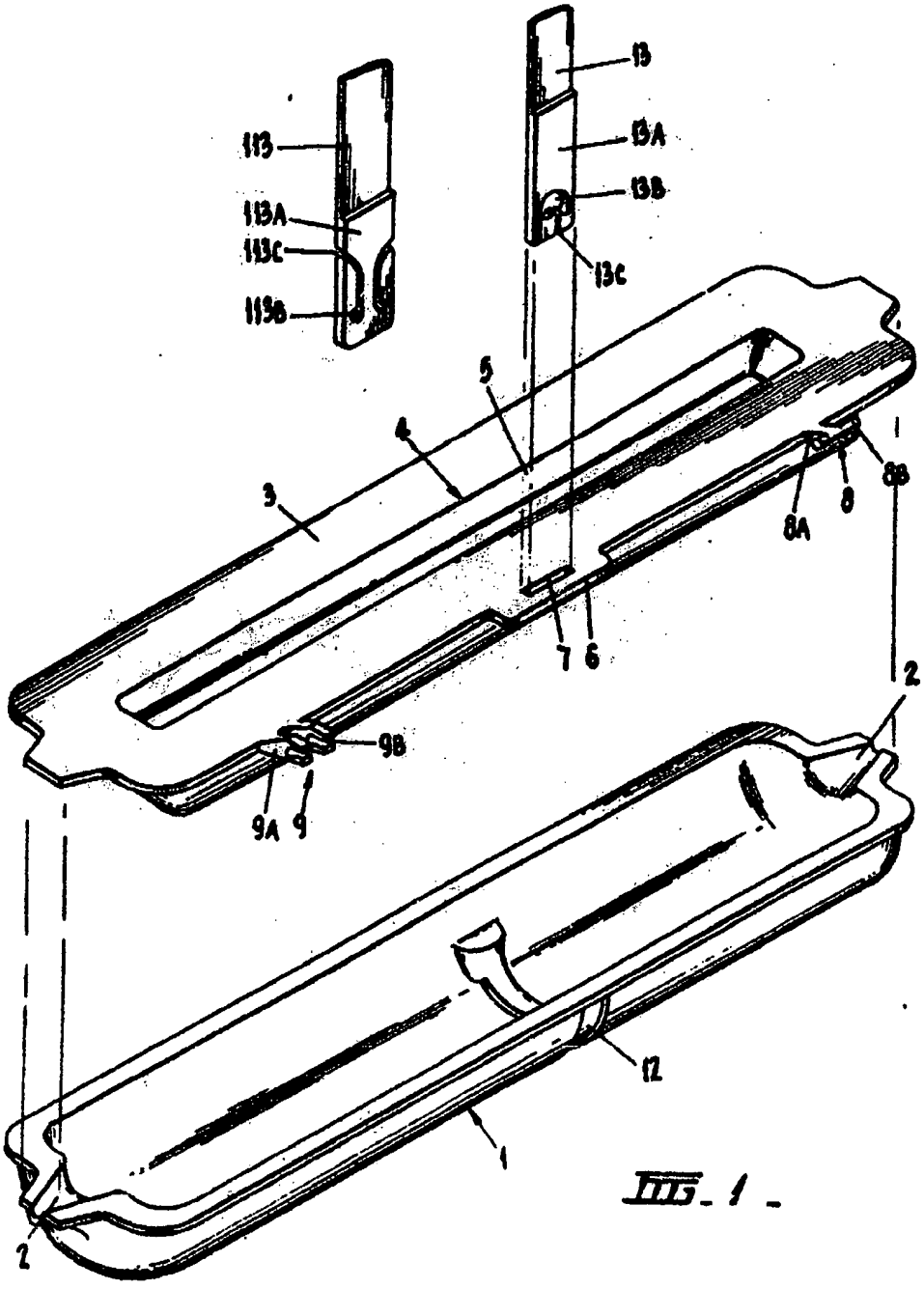
22. A method for achieving the sustained administration of a therapeutic or nutrient substance to a ruminant which comprises incorporating the said substance into a device as claimed in any one of Claims 1 to 21, and administering the device to the ruminant per os.

Dated the 2nd day of May, 1974.

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

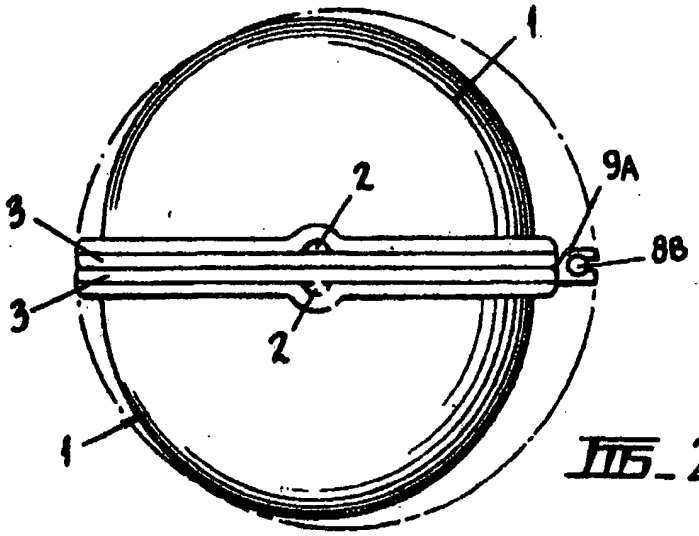
By its Patent Attorneys

DAVIES & COLLISON

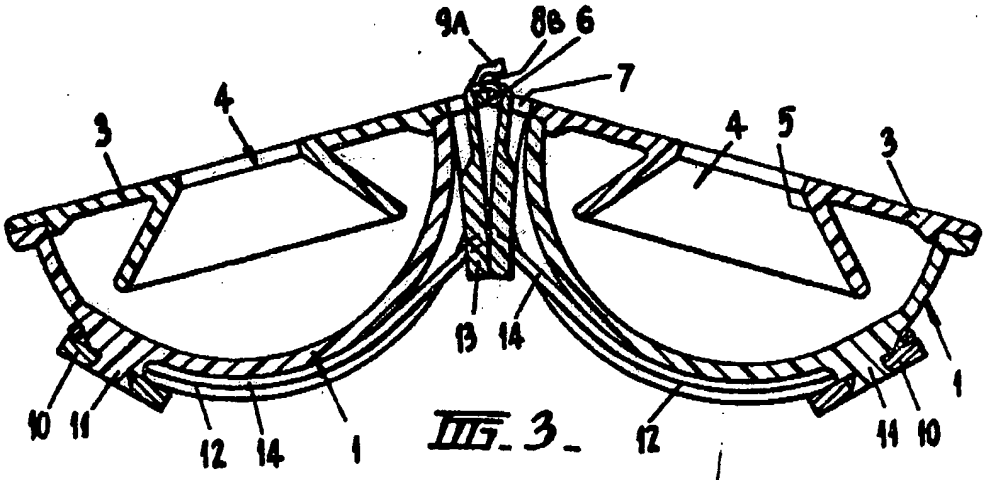


Фиг. 1

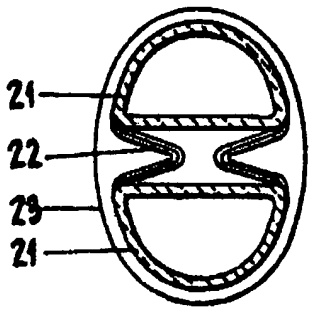
19.250 по



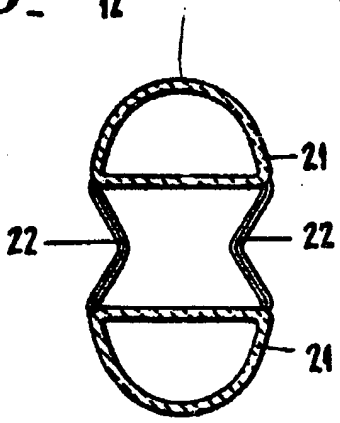
Фиг. 2.



Фиг. 3.

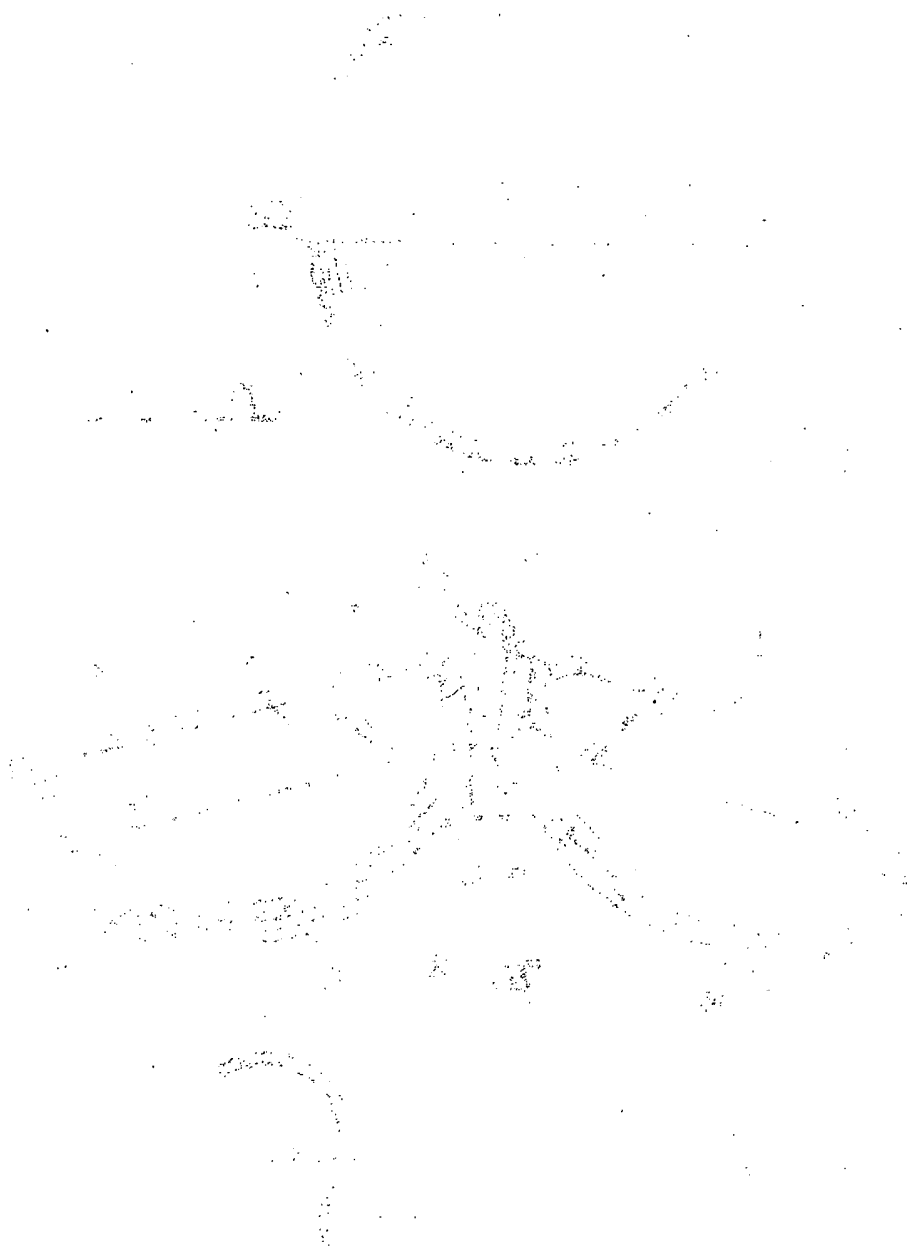


Фиг. 4.

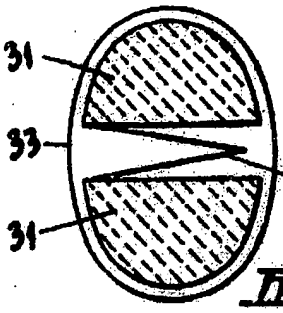


Фиг. 5.

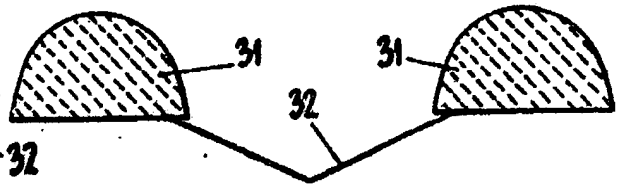
19.250 ПО



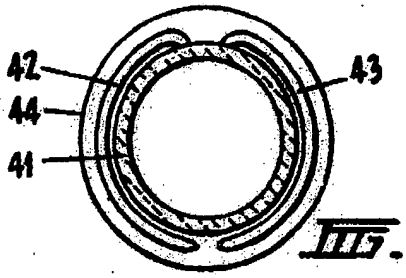
449,029



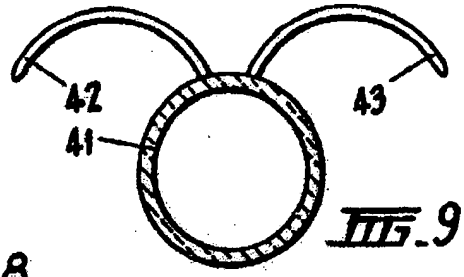
ФИГ. 6.



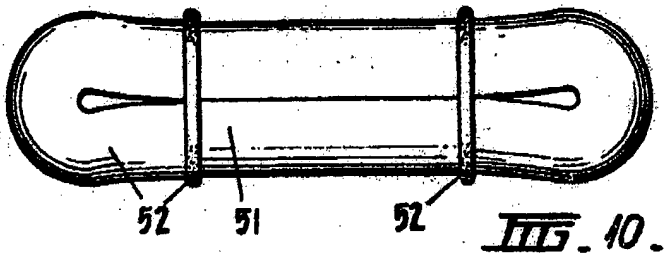
ФИГ. 7.



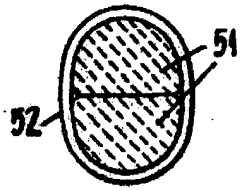
ФИГ. 8.



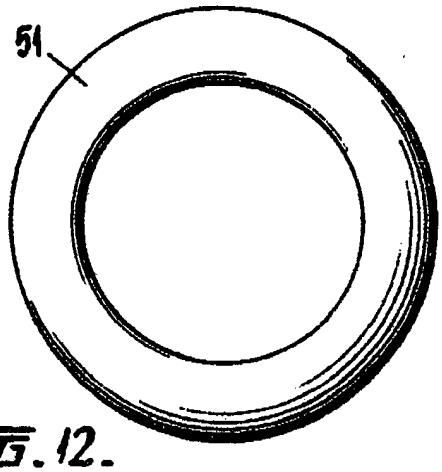
ФИГ. 9.



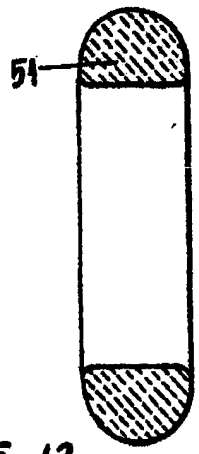
ФИГ. 10.



ФИГ. 11.



ФИГ. 12.



ФИГ. 13.

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☑ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☐ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.
As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.